First-in-Humane Phase I Study of NKTR-255 in Patients With Relapsed/Refractory Hematologic Malignancies


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BACKGROUND

NKTR-255 Engages With IL-15R/IL-2R(β) Receptor Complex to Boost NK Cell Number and CDE T Cell Expansion. Prophylaxis, Activation, Function and Survival

• NKTR-255 is a novel vaccine-like agent that can boost human natural killer (NK) cell numbers through a combination of pharmacodynamic (PD) responses and in vivo induction of IL-15R expression in patients with hematologic malignancies.

• Here we report preliminary data on safety, pharmacokinetics (PK), and biomarkers of the dose-escalation portion.

STUDY DESIGNS AND PATIENTS

Phase 1. Open-Label, Multicenter Dose-Escalation and Dose-Expansion Study in Patients With R/R MM or NHL

RESULTS

1. NKTR-255 Was Well Tolerated With No DLTs or Serious AEs (Safety Data During the DLT Period Only)

• No DLTs or serious AEs were reported.

2. NKTR-255 1.5 µg/kg Exhibited a Long Half-Life With No Accumulation After Every 21-day Dosing

• Mean plasma NKTR-255 1.5 µg/kg concentration-time profiles were superposable for cycles 1 and 2.

3. Transient Upregulation and Rapid Decline of Cytokines to Baseline Levels by Day 2 With No Further Increases

• The cytokine responses were transient, supporting the safety of NKTR-255.

4. NKTR-255 Increased Total Expansion and Proliferative Capacity (Ki67+) of NK and CDE T Cells in Blood, Peaking Around Days 8–10 Per Cycle

• The proliferative capacity of CD8+ T cells was highest in cycle 2.

5. NKTR-255 Increased Memory and Naïve CDE T Cell Subpopulations

• NKTR-255 induced CDE memory T cell expansion in all patients, including a modest increase in one patient receiving NKTR-255 1.5 µg/kg.

6. No Meaningful Changes Were Observed in CD14+ T Cells With NKTR-255 Treatment

CONCLUSIONS

• NKTR-255 was well tolerated with low-grade, cytokine-related AEs that were transient and easily managed.

• No DLTs were observed.

• No drug-related AEs led to treatment discontinuation, dose delay or dose modification.

• NKTR-255 exhibited a long half-life with no evidence of accumulation.

• NKTR-255 was biologically active and demonstrated consistent expansion of lymphocytes, with durable and sustained increases in NK and CDE T cells in this highly refractory population of patients with MM and NHL.

• These data support continued dose escalation of NKTR-255, and subsequent evaluation in combination with other anticancer agents.

REFERENCES

• The authors report relationships to the following organizations that may benefit from this study: dose escalation.

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• Crystal Mackall, MD of Stanford University and Bianca Garcia, BSN, RN of Cancer Treatment Centers of America.

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• Treatment-related AEs during the DLT period (November 2019)

• Multiple myeloma: Grade 1 and febrile symptoms (Grade 1), which were treated with antibiotics and antipyretics.

• Reproducible pattern was observed in Cycle 2, 3 and 4.

• Neutropenia Grade 0 and 0 grade 1 febrile neutropenia Grade 1 related to neutropenia Grade 1 and low platelet counts Grade 0.

• Transient transient fever resolved in order to schedule bone marrow biopsy.

• No further changes observed after Day 15.

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